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EXAMINER	
SODERQUIST, ARLEN	
ART UNIT	**PAPER NUMBER**
1743	

DATE MAILED: 06/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/086,025	ANDERSON ET AL.	
	Examin r	Art Unit	
	Arlen Soderquist	1743	

-- The MAILING DATE f this communicati n appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *109,111,113,119,120,122 and 123* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *109,111 and 113* is/are allowed.

6)☒ Claim(s) *119,120,122 and 123* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet*.

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

2. Claims 119-120 and 122-123 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lindberg (Biological Mass Spectrometry, 1992, newly cited and applied) in view of Robins (US 5,235,186, newly cited and applied), Waygood and Einarsson (newly cited and applied). In the paper Lindberg determines (22R,S)budesonide in human plasma by automated liquid chromatography/thermospray mass spectrometry. (22R,S)Budesonide was isolated from human plasma by solid-phase extraction. Switching from reversed-phase conditions during sample application and washing to normal-phase conditions during elution afforded a very clean extract. Budesonide was derivatized with acetic anhydride to form the 21-acetyl derivative before analysis by reversed-phase liquid chromatography combined with thermospray mass spectrometry. Deuterium-labeled budesonide was used as internal standard (spike). Standard samples prepared in human albumin solution were used for the calibration curve. An automated liquid chromatography/mass spectrometry system, allowing unattended overnight operation, was used for routine analysis. The recovery of budesonide from plasma was 88.9 ± 5.9% (mean ± SD) and the method was linear over the range 0.30-30 pmol (amount analyzed), corresponding to plasma concentrations of 0.10-10 nmol l^{-1}. Budesonide could be measured down to 0.10 nmol l^{-1} with a within-day variation of 10-18% (CV). The error was less than ±15% at 0.10 nmol l^{-1} and less than ±7% at concentrations of 0.20 nmol l^{-1} or higher. The total imprecision between days was 9% (CV) at a concentration of 0.30 nmol l^{-1}. Page 527, under the "Preparation of standard

solutions" heading teaches that a stock solution of the internal standard (spike) was prepared in ethanol at a concentration of 150 μmil l^{-1}. From this a working solution was prepared (by dilution) in 30% ethanol in water at a concentration of 15 nmol l^{-1}. On the same page under the "Analytical procedure" heading the addition of the diluted internal standard (spike) using a programmable (automatic) dispenser is taught. Page 528 under the "Calculations" heading teaches that the analysis is based on the ratios of the two different isotopic peaks. Lindberg does not teach an atmospheric pressure ionization method or automation of the sample preparation.

In the patent Robins teaches a probe adapter for converting a thermospray equipped LC/MS analyzer to an electrospray equipped LC/MS analyzer. Column 1, lines 43-63 teach that Electrospray Ionization (ESI) is the latest development in LC/MS interfacing and one which addresses both the ionization and mass range problems of the prior art discussed in the first part of column 1. Like Thermospray (TSP), it is a soft spray ionization technique predicated on field induced "ion evaporation" from the surface of charged liquid droplets. Both techniques nebulize the analyte containing semi-aqueous mobile phase to form an aerosol of submicron droplets from which ion evaporation occurs. ESI differs from TSP in three respects; 1) the aerosol is generated electrostatically rather than thermo-pneumatically; 2) nebulization/ionization is performed at atmospheric rather than reduced pressure; and electrostatic nebulization limits flow rates to ~ 1 to 50 mcl/min. These differences give ESI its inherently high ionization efficiency and hence mass sensitivity, its ability to produce large gas phase ions of very high charge state (m/z within instrumental mass range), and dictate the low flow regime in which the technique operates. Column 3, line 29 to column5, line 49 teach advantages of ESI compared to TSP that have motivated the inventors to provide a device that facilitates the conversion of a thermospray mass spectrometry analyzer into one capable of using electrospray technology. The problems of TSP include lower charging rates and difficulty in desolvating the ions due to the reduced pressure. The advantages of ESI include little matrix background compared to the ion clusters of TSP and a high ionization efficiency.

In the paper Waygood teaches online, real time, continuous analytical and closed loop control of process solutions for electroplating using ICP chemistry. The process of continuously electroplating steel coil with either tin or chromium, mainly for the canmaking industry, has gradually increased in speed. The strip is now processed through the various baths at speeds up

to 600 m/min. Producing material at these speeds demands extremely close tolerances upon the various process solutions. The authors have developed an automated online, real time analytical system for these process solutions. The system consists of: a large bore sampling pipeline network continuously delivering process solutions to the laboratory, an industrial robot for sampling and manipulating the samples and standard solutions, an autosampler/wash station for presenting samples to the spectrometer, a fully computerized ICP spectrometer for elemental analysis of the various process solutions. Software, specially developed is used to: interface the robot to the sampling hardware and ICP, interface the ICP analysis results to the data management system and, where appropriate, achieve closed loop control of process solution concentrations, and introduce manual samples while carrying out routine automated analysis. A full analysis of 12/13 process lines is achieved every 14 minutes, and restandardization is normally carried out automatically once every 8 hours. Current routine maintenance of the system requires ~30 min per 24 hours.

In the paper Einarsson teaches a PC-controlled module system for automatic sample preparation and analysis. A simple automatic analysis system, consisting of separate modules, for liquid chromatography was constructed. The different parts of the automatic machine are an auto sampler, an auto dispenser, a selector valve with eight channels, a heater/cooler, a mixing chamber and a pressure air driven injector valve. The process was controlled by a PC from an easily changeable run protocol. The system was applied to analysis of primary amines. The analysis was performed as a pre-column derivatization reaction of the amines and separation by isocratic reversed-phase HPLC with fluorescent detection. Reproducibility and analytical precision were studied. Comparison between automatically and manually made derivatization reaction and injection was also made. The automatic system was easy to handle, cost-effective and gave good reproducibility.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate total automation as taught by Waygood and Einarsson to automatically prepare the spike as taught by Lindberg because of the advantages for automation taught by Waygood and Einarsson or generally known in the field. It should be noted that claim 119 does not require the connection of the analyzer to the process solution. It would have been obvious to one of ordinary skill in the art at the time the invention was made to use an atmospheric pressure

ionization technique as taught by Robins for the mass spectrometric detection in the device in the Lindberg method because of the advantages taught by Robins for ESI compared to TSP.

3. Claims 109, 111 and 113 are allowed. The art of record fails to teach the combination of structure found in claim 109.

4. Applicant's arguments with respect to the claims have been considered but are moot in view of the new ground(s) of rejection. In Claim 119, there is no requirement for the various steps to be performed on a structurally coupled apparatus or for the extraction or transfer of sample or spike to be performed with the same instrument. Thus, claim 119 includes a scope covering manual transfer between the listed steps. Also, the language includes the possibility of other steps that are not claimed in addition to those that are claimed. Thus the new rejection shows the obviousness of the method claims.

5. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The additionally cited art relates to dilution apparatus and atmospheric pressure ionization.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arlen Soderquist whose telephone number is (571) 272-1265. The examiner's schedule is variable between the hours of about 6:30 AM to about 5:00 PM on Monday through Thursday and alternate Fridays.

A general phone number for the organization to which this application is assigned is (571) 272-1700. The fax phone number to file official papers for this application or proceeding is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Arlen Soderquist
Primary Examiner
June 9, 2006

Continuation of Attachment(s) 6). Other: Machine translation of Morioka (JP11-6788).

PAT-NO: JP411006788A
DOCUMENT-IDENTIFIER: JP 11006788 A
TITLE: METHOD AND DEVICE FOR AUTOMATIC PREPARATION OF SOLUTION
PUBN-DATE: January 12, 1999
INVENTOR-INFORMATION: MORIOKA, AKIHIRO; YAMANAKA, KAZUO
ASSIGNEE-INFORMATION: YOKOGAWA ANALYTICAL SYST KK
APPL-NO: JP09175146
APPL-DATE: June 17, 1997

FULL CONTENTS

[Claim(s)]

[Claim 1] A mixable apparatus is automatically used for a sample solution and the diluted solution used for attenuation of this sample solution at an arbitrary rate. The automatic preparation approach of the solution characterized by preparing the solution of the concentration higher than the concentration of the solution prepared last time in preparing the solution of at least two different concentration automatically continuously.

[Claim 2] A diluted solution storage means to store the diluted solution which is used for a sample solution storage means to store a sample solution, and attenuation of this sample solution, and contains the internal standard of prescribed concentration, A mixed means to mix a sample solution and a diluted solution, and a sample solution feed means to supply a sample solution to said mixed means from said sample solution storage means, The automatic preparation apparatus of the solution characterized by providing a means to amend the measurements based on the attenuation magnification of said sample solution, based on the concentration of the internal standard in the solution which a diluted solution feed means to supply a diluted solution to said mixed means from said diluted solution storage means, and said mixed means come to mix.

[Claim 3] A diluted solution storage means to store the diluted solution which is used for a sample solution storage means to store a sample solution, and attenuation of this sample solution, and contains the internal standard of prescribed concentration, A mixed means to mix a sample solution and a diluted solution, and a sample solution feed means to supply a sample solution to said mixed means from said sample solution storage means, A diluted solution feed means to supply a diluted solution to said mixed means from said diluted solution storage means, The automatic preparation apparatus of the solution characterized by providing a control means to control at least one action of said sample solution feed means and said diluted solution feed means, based on the concentration of the internal standard in the solution which said mixed means comes to mix.

[Claim 4] A sample solution storage means to store a sample solution, and a diluted solution storage means to store the diluted solution used for attenuation of this sample solution, The 1st mixed means which can mix a sample solution and a diluted solution, and a sample solution feed means to supply a sample solution to said 1st mixed means from said sample solution storage means, From said diluted solution storage means, to said 1st mixed means The diluted solution feed means which can supply a diluted solution, The 2nd mixed means which mixes the solution and the 1st internal standard liquid which passed a 1st internal standard liquid storage means to store the 1st internal standard liquid, and said 1st mixed means, From said 1st internal standard liquid storage means, to said 2nd mixed means The 1st internal standard liquid feed means which can supply the 1st internal standard liquid, A 2nd internal standard liquid storage means to store the 2nd internal standard liquid, and a 2nd internal standard liquid feed means to supply the 2nd internal standard liquid to the sample solution supplied to said 1st mixed means from said sample solution storage means, The automatic preparation apparatus of the solution characterized by providing a means to amend the measurements based on the attenuation magnification of said sample solution, based on the concentration of the 1st internal standard in the

solution which said 2nd mixed means comes to mix, and the 2nd internal standard.
[Claim 5] A sample solution storage means to store a sample solution, and a diluted solution storage means to store the diluted solution used for attenuation of this sample solution, The 1st mixed means which can mix a sample solution and a diluted solution, and a sample solution feed means to supply a sample solution to said 1st mixed means from said sample solution storage means, From said diluted solution storage means, to said 1st mixed means The diluted solution feed means which can supply a diluted solution, The 2nd mixed means which mixes the solution and the 1st internal standard liquid which passed a 1st internal standard liquid storage means to store the 1st internal standard liquid, and said 1st mixed means, From said 1st internal standard liquid storage means, to said 2nd mixed means The 1st internal standard liquid feed means which can supply the 1st internal standard liquid, A 2nd internal standard liquid storage means to store the 2nd internal standard liquid, and a 2nd internal standard liquid feed means to supply the 2nd internal standard liquid to the sample solution supplied to said 1st mixed means from said sample solution storage means, The automatic preparation apparatus of the solution characterized by providing a control means to control the action of said diluted solution feed means, based on the concentration of the 1st internal standard in the solution which said 2nd mixed means comes to mix, and the 2nd internal standard.
[Claim 6] Each above-mentioned feed means is the automatic preparation apparatus of a solution given in any of Claim 2 or Claim 5 which are characterized by being a peri pump they are.

[Detailed Description of the Invention]
[0001]
[Field of the Invention] Especially this invention relates to the apparatus used for the approach and it which dilute an undiluted solution and prepare the sample solution of the predetermined attenuation magnification about the automatic preparation approaches of a solution, and automatic preparation apparatus. For example, it applies to automatic production of the sample solution for high frequency inductively coupled plasma and a mass spectroscope (ICP-MS is called hereafter), or high frequency inductively coupled plasma and quantometers (ICP-AES), and is related with a useful technique.
[0002]
[Description of the Prior Art] The sample tub in which drawing 4 is an overall example of an architecture figure of said ICP-MS, and 1a is storing the solution to be measured among drawing, 1b For example, the pump with which the tub which is storing a solvent like pure water, 2a, and 2b send out a solution to be measured and a solvent, respectively, The controller by which 3 controls Pump 2a and the amount of sending out of 2b, the computer by which 4 sends a command signal to a controller, The atomization introduction apparatus of the sample solution which consists of a nebulizer 500 and a spray chamber 510 with which 5 gasifies Pump 2a and the test portion supplied from 2b, The pressure regulator with which 6 adjusts a plasma torch, 7a adjusts an argon gas supply source, and 7b adjusts the pressure of argon gas, The high frequency power source with which 8 supplies the high frequency derivation plasma, 9 supplies a high frequency induction coil, and 10 supplies high frequency energy to said high frequency induction coil 9, As for a chamber, 14, 16, and 19, a discharge jet and 12 are [secondary-electron redoubling tubing and 21] signal-processing parts like a microcomputer a skimmer, 13, 15, and 18 11 a vacuum pump, a pole [like for example, a quadrupole mass filter] whose 17 is, and 20.
[0003] In ICP-MS of this architecture, the test portion gasified by the atomization introduction apparatus 5 of the sample solution is supplied and excited by the plasma torch 6, and is ionized in an operation of the high frequency derivation plasma 8. The ionized test portion is led to a mass spectrometer through a discharge jet 11 and a skimmer 12, and quality and a quantitative analysis are carried out here.
[0004] It is die RYUTA of the former and Gilson as the apparatus which prepares the test portion liquid supplied to such an analyses apparatus, i.e., an attenuation apparatus which dilutes the undiluted solution of the solution used as a test portion with pure water etc., and obtains the solution of the desired attenuation magnification. Model There is 401. This die RYUTA Model When they prepares test portion

liquid, each of 401 and other well-known attenuation apparatus leaves an undiluted solution, produces a high-concentration sample solution first, is diluted further and produces a low-concentration sample solution gradually. that is, in analyzing a sample solution generally First For example, after analyzing by preparing a sample solution with a concentration (high concentration) of 1000 ppm, The procedure of analyzing by diluting furthermore, for example, analyzing by preparing a sample solution with a concentration (inside concentration) of 50 ppm, and diluting further after that, for example, preparing a sample solution with a concentration (low concentration) of 1 ppm is analyzing. It is because it is very difficult to obtain a further high-concentration sample solution from a high-concentration undiluted solution compared with this diluting a high-concentration undiluted solution gradually, and obtaining the sample solution of the concentration of a request.

[0005]

[Problem to be solved by the invention] However, in order to produce low-concentration test portion liquid gradually from high-concentration test portion liquid with the above-mentioned conventional attenuation apparatus, Since many high concentration sample solutions will be measured in early stages of analyses when this attenuation apparatus is applied, for example to automatic preparation and feed of the sample solution in analyses apparatus, such as ICP-MS, There was a problem that will get the discharge jet and skimmer of ICP-MS blocked, or degradation of electronic redoubling tubing of ICP-MS will become intense, and a life will become short. Moreover, in the case of what is called on-line equipment that adds pure water etc. to the undiluted solution of a sample solution, produces the solution of the concentration of a request, and is automatically supplied to an analyses apparatus, there was also a problem [produce / the solution of the desired attenuation magnification / it is impossible to get to know the attenuation magnification correctly, therefore / correctly] of being unknown. Furthermore, since the attenuation magnification changed by degradation of the tube which is the channel of a solution etc. in the case of the attenuation apparatus using the peri pump as a feed means to send out a solution, there was also a problem that it was very difficult to set up the exact attenuation magnification beforehand.

[0006] This invention was made in order to solve the above-mentioned trouble, and it aims at offering the automatic preparation approaches of the solution in which automatic production of the sample solution to high concentration [low concentration] is possible. Moreover, other objects of this invention are to offer the attenuation apparatus using the peri pump which the attenuation magnification can be known correctly, and the solution of the desired attenuation magnification can be obtained with sufficient accuracy by it, and can set up the attenuation magnification still more correctly.

[0007]

[Means for solving problem] Invention indicated to Claim 1 uses a mixable apparatus for a sample solution and the diluted solution used for attenuation of this sample solution automatically at an arbitrary rate. In preparing the solution of at least two different concentration automatically continuously, it is characterized by preparing the solution of concentration higher than the concentration of the solution prepared last time.

[0008] Since according to this invention a low-concentration solution is left and a solution with high concentration is produced gradually While the discharge jet of ICP-MS and ****** of a skimmer are prevented by conducting the analyses in ICP-MS with the application of the automatic preparation approaches of this solution, the ephemeralization by degradation of electronic redoubling tubing of ICP-MS is prevented.

[0009] A diluted solution storage means to store the diluted solution which invention indicated to Claim 2 is used for a sample solution storage means to store a sample solution, and attenuation of this sample solution, and contains the internal standard of prescribed concentration, A mixed means to mix a sample solution and a diluted solution, and a sample solution feed means to supply a sample solution to said mixed means from said sample solution storage means, It is characterized by providing a means to amend the measurements based on the attenuation magnification of said sample solution, based on the concentration of the internal standard in the solution which a diluted solution feed means to supply a

diluted solution to said mixed means from said diluted solution storage means, and said mixed means come to mix.

[0010] According to this invention, the attenuation magnification of the produced solution can be correctly known by measuring the concentration of the internal standard in the produced solution, and amending the measurements based on the attenuation magnification of a sample solution.

[0011] A diluted solution storage means to store the diluted solution which invention indicated to Claim 3 is used for a sample solution storage means to store a sample solution, and attenuation of this sample solution, and contains the internal standard of prescribed concentration, A mixed means to mix a sample solution and a diluted solution, and a sample solution feed means to supply a sample solution to said mixed means from said sample solution storage means, A diluted solution feed means to supply a diluted solution to said mixed means from said diluted solution storage means, It is characterized by providing a control means to control at least one action of said sample solution feed means and said diluted solution feed means, based on the concentration of the internal standard in the solution which said mixed means comes to mix.

[0012] Since an action of either a sample solution feed means or a diluted solution feed means and both is controlled based on the measured internal standard according to this invention, the solution of the desired attenuation magnification is always produced.

[0013] A sample solution storage means by which invention indicated to Claim 4 stores a sample solution, and a diluted solution storage means to store the diluted solution used for attenuation of this sample solution, The 1st mixed means which can mix a sample solution and a diluted solution, and a sample solution feed means to supply a sample solution to said 1st mixed means from said sample solution storage means, From said diluted solution storage means, to said 1st mixed means The diluted solution feed means which can supply a diluted solution, The 2nd mixed means which mixes the solution and the 1st internal standard liquid which passed a 1st internal standard liquid storage means to store the 1st internal standard liquid, and said 1st mixed means, From said 1st internal standard liquid storage means, to said 2nd mixed means The 1st internal standard liquid feed means which can supply the 1st internal standard liquid, A 2nd internal standard liquid storage means to store the 2nd internal standard liquid, and a 2nd internal standard liquid feed means to supply the 2nd internal standard liquid to the sample solution supplied to said 1st mixed means from said sample solution storage means, It is characterized by providing a means to amend the measurements based on the attenuation magnification of said sample solution, based on the concentration of the 1st internal standard in the solution which said 2nd mixed means comes to mix, and the 2nd internal standard.

[0014] The attenuation magnification of the produced solution can be correctly known by measuring the concentration of the 1st and 2nd internal standards in the produced solution according to this invention, and amending the measurements based on the attenuation magnification of a sample solution.

[0015] A sample solution storage means by which invention indicated to Claim 5 stores a sample solution, and a diluted solution storage means to store the diluted solution used for attenuation of this sample solution, The 1st mixed means which can mix a sample solution and a diluted solution, and a sample solution feed means to supply a sample solution to said 1st mixed means from said sample solution storage means, From said diluted solution storage means, to said 1st mixed means The diluted solution feed means which can supply a diluted solution, The 2nd mixed means which mixes the solution and the 1st internal standard liquid which passed a 1st internal standard liquid storage means to store the 1st internal standard liquid, and said 1st mixed means, From said 1st internal standard liquid storage means, to said 2nd mixed means The 1st internal standard liquid feed means which can supply the 1st internal standard liquid, A 2nd internal standard liquid storage means to store the 2nd internal standard liquid, and a 2nd internal standard liquid feed means to supply the 2nd internal standard liquid to the sample solution supplied to said 1st mixed means from said sample solution storage means, It is characterized by providing a control means to control the action of said diluted solution feed means, based on the concentration of the 1st internal standard in the solution which said 2nd mixed means comes to mix, and the 2nd internal standard.

[0016] Since the action of a diluted solution feed means is controlled based on the measured internal standard according to this invention, the solution of the desired attenuation magnification is always produced.
[0017] Invention indicated to Claim 6 is characterized by each above-mentioned feed means being a peri pump in invention according to claim 2, 3, 4, or 5.
[0018] According to this invention, in the attenuation apparatus using the peri pump as a feed means to send out a solution, the action of a diluted solution feed means is controlled based on the internal standard which could know the attenuation magnification of the produced solution correctly, and was measured. For this reason, it becomes possible to set up the attenuation magnification correctly beforehand.
[0019]
[Mode for carrying out the invention] It explains in detail, referring to drawing 1 - drawing 3 about the form of operation of this invention below. The outline of one embodiment applied to the on-line attenuation apparatus which prepares the sample solution of the desired attenuation magnification automatically, and supplies the automatic preparation apparatus of the solution concerning this invention to ICP-MS is shown in drawing 1 .
[0020] The sample solution tub 100 which is a sample solution storage means by which this solution automatic preparation apparatus stores a sample solution (undiluted solution), The 1st peri pump 105 which is a sample solution feed means to send out a sample solution from the sample solution tub 100, The diluted solution tub 110 which is a diluted solution storage means to store the diluted solution which consists of pure water etc., The 2nd peri pump 115 which is a diluted solution feed means to send out a diluted solution from the diluted solution tub 110, The 1st connector 120 which makes the sample solution and diluted solution which were sent out with them 1st and the 2nd peri pump 105,115, respectively join the same channel, The mixing loop formation 130 which is the mixed means which uses as a uniform mixed solution the sample solution and diluted solution which joined by the connector 120, The 2nd connector 125 which the atomization introduction apparatus 5 and the abolition tub (depot for abolition) 170 of a sample solution which consist of the nebulizer and spray chamber of ICP-MS are branched, and pours the solution uniformly mixed by the mixing loop formation 130, The 3rd peri pump 140 which pours a sample solution from the connector 125 to the atomization introduction apparatus 5, and the sample solution discharged from the atomization introduction apparatus 5 The 4th peri pump 150 of abolition tub 170 HE ****, The abolition tub side HE flow ******** was made to join from the sample solution sent from the atomization introduction apparatus 5 through the peri pump 150, and the 2nd connector 125, and it has abolition tub 170 HE style **** 3 connector 128.
[0021] Moreover, the control means 160 which becomes this solution automatic preparation apparatus from the controller which controls actuation, rundown, and rotating speed of at least one revolution action of the 1st and 2nd peri pumps 105,115, and the computer which controls that controller is established.
[0022] The channel between the sample solution tub 100 and the 1st connector 120, the channel between the diluted solution tub 110 and the 1st connector 120, The channel between the 2nd connector 125 and the atomization introduction apparatus 5, the channel between the atomization introduction apparatus 5 and the 3rd connector 128, The channel between the 2nd connector 125 and the 3rd connector 128 and the channel between the 3rd connector 128 and the abolition tub 170 are constituted by the tube for for example, peri pumps etc., respectively. In addition, the flow of a sample solution and a diluted solution and the hand of cut of each pump are shown to drawing 1 by the arrow head.
[0023] In the diluted solution in said diluted solution tub 110, the internal standard of prescribed concentration contains beforehand. And the concentration of the internal standard in the diluted sample solution is detected by ICP-MS, and rotation of one side of the 1st and 2nd peri pumps 105,115 or both is controlled by the control means 160 based on the detection result. In addition, the concentration of an internal standard is checked with the record value and indicated value of the output of electronic redoubling tubing of ICP-MS, the recorder connected to ICP-MS, or a display device.

[0024] The operation of the solution automatic preparation apparatus of architecture of being shown in drawing 1 is as follows. [the sample solution (undiluted solution) sent out by rotation of the peri pump 105 from the sample solution tub 100] It joins through a connector 120, it is uniformly mixed with the diluted solution (the internal standard of prescribed concentration is included) sent out by rotation of the peri pump 115 from the diluted solution tub 110 through the mixing loop formation 130, and becomes the test portion liquid of the predetermined attenuation magnification. The sample solution branches to two channels through a connector 125. The sample solution which branched to the atomization introduction apparatus side is sent to the atomization introduction apparatus 5 with the peri pump 140, and analyses by ICP-MS are presented with it.
[0025] The concentration of the internal standard in a sample solution is also detected in that case. And the operation of whether based on the concentration of the detected internal standard, the sample solution which was sent to the atomization introduction apparatus 5 and with which analyses were presented had become the predetermined attenuation magnification is performed in the computer of the control means 160. Based on the operation result, rotation of one side of the 1st and 2nd peri pumps 105,115 or both is controlled to become the predetermined attenuation magnification.
[0026] On the other hand, the sample solution which branched to the abolition tub side in the connector 125 joins the analyzed sample solution sent from the atomization introduction apparatus 5 with the peri pump 150 in a connector 128, and is abolition tub 170 HE ********.
[0027] According to the above-mentioned embodiment, the internal standard of prescribed concentration is contained in a diluted solution, and since the concentration of the internal standard in the sample solution which it comes to dilute with the diluted solution was detected, the attenuation magnification of the sample solution with which analyses were presented can be known correctly. Moreover, according to the above-mentioned embodiment, get to know correctly the attenuation magnification of the sample solution with which analyses were presented, and based on the value of the obtained attenuation magnification [with the control means 160] Since an action of one side of the peri pump 115 or both which send out the peri pump 105 and diluted solution which send out a sample solution is controlled, the sample solution of the desired attenuation magnification is always obtained.
[0028] The outline of other embodiments applied to the on-line attenuation apparatus which prepares the sample solution of the desired attenuation magnification automatically, and supplies the automatic preparation apparatus of the solution concerning this invention to ICP-MS is shown in drawing 2 .
[0029] The sample solution tub (sample solution storage means) 100 in which this solution automatic preparation apparatus stores a sample solution (undiluted solution), The 1st peri pump (sample solution feed means) 105 which sends out a sample solution from the sample solution tub 100, The diluted solution tub (diluted solution storage means) 110 which stores the diluted solution which consists of pure water etc., The 2nd peri pump (diluted solution feed means) 115 which sends out a diluted solution from the diluted solution tub 110, The 1st connector 120 which makes the sample solution and diluted solution which were sent out with them 1st and the 2nd peri pump 105,115, respectively join the same channel, The 1st mixing loop formation (1st mixed means) 130 which uses as a uniform mixed solution the sample solution and diluted solution which joined by the connector 120, The 2nd connector 125 which the atomization introduction apparatus 5 and the abolition tub 170 of a sample solution which consist of the nebulizer and spray chamber of ICP-MS are branched, and pours the solution uniformly mixed by the mixing loop formation 130, The 3rd peri pump 140 which pours a sample solution from the connector 125 to the atomization introduction apparatus 5, and the sample solution discharged from the atomization introduction apparatus 5 The 4th peri pump 150 of abolition tub 170 HE ****, The abolition tub side HE flow ******** was made to join from the sample solution sent from the atomization introduction apparatus 5 through the peri pump 150, and the 2nd connector 125, and it has abolition tub 170 HE style **** 3 connector 128.
[0030] moreover, [this solution automatic preparation apparatus] [the 1st internal standard liquid sent out with the 5th peri pump 205 which is a 1st internal standard liquid feed means to send out the 1st internal standard liquid from the 1st internal standard cistern 200 which is a 1st internal standard liquid

storage means to store the 1st internal standard liquid, and the 1st internal standard cistern 200, and the 5th peri pump 205] [with the 4th connector 220 made to join the sample solution which passes the 1st mixing loop formation 130 and is supplied to the atomization introduction apparatus 5, and its connector 220] [the sample solution and the 1st internal standard liquid which joined] The 2nd mixing loop formation used as a uniform mixed solution (2nd mixed means) [cistern / 210 / 230, the 2nd internal standard cistern 210 which is a 2nd internal standard liquid storage means to store the 2nd internal standard liquid, and / 2nd internal standard / with the 6th peri pump 215 and the 6th peri pump 215 which are a 2nd internal standard liquid feed means to send out the 2nd internal standard liquid] The 3rd mixing loop formation 235 which uses the 5th connector 225 which makes the sample solution sent out from the sample solution tub 100 mix the 2nd sent-out internal standard liquid, the sample solution which joined by the connector 225, and the 2nd internal standard liquid as a uniform mixed solution is established.

[0031] Furthermore, the control means 260 which becomes this solution automatic preparation apparatus from the controller which controls actuation, rundown, and rotating speed of a revolution action of the 2nd peri pump 115, and the computer which controls that controller is established.

[0032] The 1st peri pump 105, the 3rd peri pump 140, the 4th peri pump 150, the 5th peri pump 205, and the 6th peri pump 215 are always rotating with a fixed rotating speed, while preparing the sample solution. Moreover, as mentioned above, drive controlling of the 2nd peri pump 115 is carried out by the control means 260, and the rotating speed serves as adjustable.

[0033] Each channel between the sample solution tub 100 and the 2nd internal standard cistern 210, and the 5th connector 225, The channel between the 3rd mixing loop formation 235 and the 1st connector 120, Each channel between the channel between the diluted solution tub 110 and the 1st connector 120, the 2nd connector 125, and the 1st internal standard cistern 200 and the 4th connector 220, The channel between the atomization introduction apparatus 5 and the 3rd connector 128, the channel between the 2nd connector 125 and the 3rd connector 128, and the channel between the 3rd connector 128 and the abolition tub 170 are constituted by the tube for for example, peri pumps etc., respectively. In addition, the flow of a sample solution, a diluted solution, and each internal standard liquid and the hand of cut of each pump are shown to drawing 2 by the arrow head.

[0034] The concentration of the 1st and 2nd internal standards in the sample solution supplied to the atomization introduction apparatus 5 is detected by ICP-MS, and rotation of the 2nd peri pump 115 is controlled by this solution automatic preparation apparatus by the control means 260 based on the detection result of the 2nd internal standard. Make it rotate and stop by the control means 260, and the 2nd peri pump 115 specifically The detected strength (namely, when having added the 2nd internal standard to the sample solution) of the 2nd internal standard at the time of a revolution, The attenuation magnification of a sample solution is obtained by measuring the detected strength of the 2nd internal standard at the time of a revolution rundown (namely, when not having added the 2nd internal standard to a sample solution). Moreover, about the detected strength of the 2nd internal standard, it amends with the detected strength of the 1st internal standard. In addition, it is checked with the record value and indicated value of the output of electronic redoubling tubing of ICP-MS, the recorder connected to ICP-MS, or a display device, the reinforcement, i.e., the concentration, of each internal standard.

[0035] The operation of the solution automatic preparation apparatus of architecture of being shown in drawing 2 is as follows. [the sample solution (undiluted solution) sent out by rotation of the peri pump 105 from the sample solution tub 100] The 2nd internal standard liquid sent out by rotation of the peri pump 215 from the 2nd internal standard cistern 210, It joins through a connector 225 and the mixing loop formation 235 is mixed uniformly, and it joins through a connector 120 and is uniformly mixed with the diluted solution further sent out by rotation of the peri pump 115 from the diluted solution tub 110 through the mixing loop formation 130. The mixed sample solution branches to two channels through a connector 125. The sample solution which branched to the atomization introduction apparatus side joins the 1st internal standard liquid sent out by rotation of the peri pump 205 from the 1st internal standard cistern 200 through the peri pump 140 and a connector 220, and is uniformly mixed through the

mixing loop formation 230. The mixed sample solution is sent to the atomization introduction apparatus 5, and analyses by ICP-MS are presented with it.
[0036] The concentration of the internal standard in a sample solution is also detected in that case. And the operation of whether as mentioned above, based on the concentration of the detected internal standard, the sample solution which was sent to the atomization introduction apparatus 5 and with which analyses were presented had become the predetermined attenuation magnification is performed in the computer of the control means 260. Based on the operation result, rotation of the 2nd peri pump 115 is controlled to become the predetermined attenuation magnification.
[0037] On the other hand, the sample solution which branched to the abolition tub side in the connector 125 joins the analyzed sample solution sent from the atomization introduction apparatus 5 with the peri pump 150 in a connector 128, and is abolition tub 170 HE ********.
[0038] According to the 2nd embodiment of the above, a sample solution is made to mix the internal standard of prescribed concentration, and since the concentration of the internal standard in the sample solution which it comes to dilute with a diluted solution was detected, the attenuation magnification of the sample solution with which analyses were presented can be known correctly. Moreover, according to the 2nd embodiment of the above, the attenuation magnification of the sample solution with which analyses were presented is got to know correctly, and since the action of the peri pump 115 which sends out a diluted solution is controlled by the control means 260 based on the value of the obtained attenuation magnification, the sample solution of the desired attenuation magnification is obtained.
[0039] An example of the flow of the preparation approaches of the sample solution in the solution automatic preparation apparatus shown in drawing 1 or drawing 2 is shown in drawing 3 . By the preparation approaches of the sample solution concerning this invention, first, a low-concentration (for example, 1 ppm) sample solution is prepared automatically, and is supplied to analyses apparatus, such as ICP-MS, (step S1). And it is judged whether the limit of detection (analyses lower limit) of the analyses apparatus was exceeded (step S2). At step S2, when the concentration of the element of the request in "Yes, i.e., a sample solution," can be normally measured now, preparing the sample solution of step S6 HE progress and its concentration is continued, and it is continuously supplied to an analyses apparatus.
[0040] On the other hand, at step S2, the concentration of the element of the request in "No, i.e., a sample solution," is below an analyses lower limit, and when the concentration cannot be measured normally, the sample solution of inside concentration (for example, 50 ppm) is prepared automatically, and is supplied to analyses apparatus, such as ICP-MS, (step S3). And it is judged whether the limit of detection (analyses lower limit) of the analyses apparatus was exceeded (step S4). At step S4, when the concentration of the element of the request in "Yes, i.e., a sample solution," can be normally measured now, preparing the sample solution of step S6 HE progress and its concentration is continued, and it is continuously supplied to an analyses apparatus.
[0041] On the other hand when the concentration of the element of the request in "No, i.e., a sample solution," is below an analyses lower limit and the concentration cannot be normally measured at step S4 The high-concentration (for example, 1000 ppm) sample solution exceeding an analyses lower limit is prepared automatically, and is supplied succeeding analyses apparatus, such as ICP-MS, (step S5, S6).
[0042] What is necessary is to change automatically the feed rate of the undiluted solution of a sample solution, and a diluted solution by the drive controlling of the peri pump by the control means 160,260, and just to make it mix in the apparatus shown in drawing 1 or drawing 2 as an approach of raising the concentration of the sample solution supplied to an analyses apparatus one by one. Or you may make it evaporate the moisture in a mixed solution by heating the mixed solution of the undiluted solution of a sample solution, and a diluted solution using a heater etc.
[0043] Since according to the preparation approaches of this sample solution a low concentration sample is left and a sample with high concentration is gradually produced, as mentioned above For example, when conducting the analyses in ICP-MS, while the discharge jet of ICP-MS and ****** of a skimmer are prevented, the ephemeralization by degradation of electronic redoubling tubing of ICP-MS is

prevented.
[0044] in addition, [solution automatic preparation apparatus] not only in the thing of architecture of being shown in drawing 1 and drawing 2 It cannot be overemphasized that can change variously, if an internal standard can be mixed in the sample solution supplied to an analyses apparatus, the attenuation magnification of a sample solution can be correctly known by detecting the concentration of the internal standard, it can be fed back and the attenuation magnification can be controlled with sufficient accuracy. For example, each feed means to convey a sample solution, a diluted solution, and each internal standard may be the pump of not only a peri pump but other formats etc. Moreover, although [drawing 3] a sample solution is produced by the concentration of a three-stage, it is good as two steps and the concentration of a sample solution is also as four or more steps, and it is **. Furthermore, this invention can be applied when preparing automatically not only when preparing the sample solution for ICP-MS automatically but other analyses apparatus, and the solution of request concentration or the solution of the desired attenuation magnification used for applications other than analyses.
[0045]
[Effect of the Invention] According to invention according to claim 1, a mixable apparatus is automatically used for a sample solution and the diluted solution used for attenuation of this sample solution at an arbitrary rate. Since a low-concentration solution is left and a solution with high concentration is gradually produced, in order to prepare the solution of concentration higher than the concentration of the solution prepared last time in preparing the solution of at least two different concentration automatically continuously While the discharge jet of ICP-MS and ****** of a skimmer are prevented by conducting the analyses in ICP-MS with the application of the automatic preparation approaches of this solution, the ephemeralization by degradation of electronic redoubling tubing of ICP-MS is prevented.
[0046] A sample solution storage means to store a sample solution according to invention according to claim 2, A diluted solution storage means to store the diluted solution which is used for attenuation of this sample solution, and contains the internal standard of prescribed concentration, A mixed means to mix a sample solution and a diluted solution, and a sample solution feed means to supply a sample solution to said mixed means from said sample solution storage means, Since a means to amend the measurements based on the attenuation magnification of said sample solution is provided based on the concentration of the internal standard in the solution which a diluted solution feed means to supply a diluted solution to said mixed means from said diluted solution storage means, and said mixed means come to mix, The attenuation magnification of the produced solution can be correctly known by measuring the concentration of the internal standard in the produced solution, and amending the measurements based on the attenuation magnification of a sample solution.
[0047] A sample solution storage means to store a sample solution according to invention according to claim 3, A diluted solution storage means to store the diluted solution which is used for attenuation of this sample solution, and contains the internal standard of prescribed concentration, A mixed means to mix a sample solution and a diluted solution, and a sample solution feed means to supply a sample solution to said mixed means from said sample solution storage means, A diluted solution feed means to supply a diluted solution to said mixed means from said diluted solution storage means, Since a control means to control at least one action of said sample solution feed means and said diluted solution feed means is provided based on the concentration of the internal standard in the solution which said mixed means comes to mix, Since an action of either a sample solution feed means or a diluted solution feed means and both is controlled based on the measured internal standard, the solution of the desired attenuation magnification is always produced.
[0048] A sample solution storage means to store a sample solution according to invention according to claim 4, A diluted solution storage means to store the diluted solution used for attenuation of this sample solution, The 1st mixed means which can mix a sample solution and a diluted solution, and a sample solution feed means to supply a sample solution to said 1st mixed means from said sample solution storage means, From said diluted solution storage means, to said 1st mixed means The diluted solution

feed means which can supply a diluted solution, The 2nd mixed means which mixes the solution and the 1st internal standard liquid which passed a 1st internal standard liquid storage means to store the 1st internal standard liquid, and said 1st mixed means, From said 1st internal standard liquid storage means, to said 2nd mixed means The 1st internal standard liquid feed means which can supply the 1st internal standard liquid, A 2nd internal standard liquid storage means to store the 2nd internal standard liquid, and a 2nd internal standard liquid feed means to supply the 2nd internal standard liquid to the sample solution supplied to said 1st mixed means from said sample solution storage means, It is based on the concentration of the 1st internal standard in the solution which said 2nd mixed means comes to mix, and the 2nd internal standard. By measuring the concentration of the 1st and 2nd internal standards in the solution produced since a means to amend the measurements based on the attenuation magnification of said sample solution was provided, and amending the measurements based on the attenuation magnification of a sample solution [0049] which can know the attenuation magnification of the produced solution correctly A sample solution storage means to store a sample solution according to invention according to claim 5, A diluted solution storage means to store the diluted solution used for attenuation of this sample solution, The 1st mixed means which can mix a sample solution and a diluted solution, and a sample solution feed means to supply a sample solution to said 1st mixed means from said sample solution storage means, From said diluted solution storage means, to said 1st mixed means The diluted solution feed means which can supply a diluted solution, The 2nd mixed means which mixes the solution and the 1st internal standard liquid which passed a 1st internal standard liquid storage means to store the 1st internal standard liquid, and said 1st mixed means, From said 1st internal standard liquid storage means, to said 2nd mixed means The 1st internal standard liquid feed means which can supply the 1st internal standard liquid, A 2nd internal standard liquid storage means to store the 2nd internal standard liquid, and a 2nd internal standard liquid feed means to supply the 2nd internal standard liquid to the sample solution supplied to said 1st mixed means from said sample solution storage means, Since a control means to control the action of said diluted solution feed means is provided based on the concentration of the 1st internal standard in the solution which said 2nd mixed means comes to mix, and the 2nd internal standard, Since the action of a diluted solution feed means is controlled based on the measured internal standard, the solution of the desired attenuation magnification is always produced.
[0050] According to invention according to claim 6, in the attenuation apparatus using the peri pump as a feed means to send out a solution, the action of a diluted solution feed means is controlled based on the internal standard which could know the attenuation magnification of the produced solution correctly, and was measured. For this reason, it becomes possible to set up the attenuation magnification correctly beforehand.

[Brief Description of the Drawings]
[Drawing 1] It is the schematic diagram showing the 1st embodiment of the automatic preparation apparatus of the solution concerning this invention.
[Drawing 2] It is the schematic diagram showing the 2nd embodiment of the automatic preparation apparatus of the solution concerning this invention.
[Drawing 3] It is the flowchart which shows an example of the automatic preparation approaches of the solution concerning this invention.
[Drawing 4] It is the schematic diagram of ICP-MS.
[Explanations of letters or numerals]
5 Atomization Introduction Apparatus
100 Sample Solution Tub (Sample Solution Storage Means)
105 1st Peri Pump (Sample Solution Feed Means)
110 Diluted Solution Tub (Diluted Solution Storage Means)
115 2nd Peri Pump (Diluted Solution Feed Means)
120 1st Connector
125 2nd Connector

128 3rd Connector
130 Mixing Loop Formation (Mixed Means)
140 3rd Peri Pump
150 4th Peri Pump
160,260 Control means
170 Abolition Tub
200 1st Internal Standard Cistern (1st Internal Standard Liquid Storage Means)
205 5th Peri Pump (1st Internal Standard Liquid Feed Means)
210 2nd Internal Standard Cistern (2nd Internal Standard Liquid Storage Means)
215 6th Peri Pump (2nd Internal Standard Liquid Feed Means)
220 4th Connector
225 5th Connector
230 2nd Mixing Loop Formation (2nd Mixed Means)
235 3rd Mixing Loop Formation
